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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/595,122

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EXAMINER

CHUNG, SUSANNAH LEE

ART UNIT

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1626

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/595,122	Applicant(s) ITAYA ET AL.	
	Examiner Susannah Chung	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 December 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/1/06, 12/4/08</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-12 are pending in the instant application.

Priority

This application is a 371 of PCT/JP04/13014, filed 09/01/2004.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) by application no. 2003-313325 filed in the Japanese Patent Office on 9/4/2003, which papers have been placed of record in the file. The application names an inventor or inventors named in the prior application.

Information Disclosure Statement

The information disclosure statements (IDS), filed on 11/1/06 and 12/4/08 have been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are incomplete because they omit essential steps, such omission amounting to a gap between the steps. See MPEP §2172.01. The omitted steps are the reagents used and specific steps of preparing the intermediate of valsartan. Applicants need to include specific reagents and steps as described in the specification on page 5 for example. The process is incomplete. It is acknowledged that there are one-step processes, but the instantly claimed

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reaction as depicted on page 5 for example shows that there are at least two essential steps, i.e. the purification step is missing.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being obvious over Daumas et al (US Patent No. 5,371,233 ('233 Pat)).

Claim 11 relates to highly pure crystal of 2'-(1H-tetrazol-5-yl)biphenyl-4-carbaldehyde substantially containing no 2'-(1H-tetrazol-5-yl)biphenyl-4-carboxylic acid and a crystal with a particular x-ray diffraction pattern.

Claim 12 relates to highly pure crystal of 2'-(1H-tetrazol-5-yl)biphenyl-4-carbaldehyde with peaks at 9.2, 20.6, 25.7, and 26.9 by x-ray diffraction pattern.

Determination of the scope and content of the prior art (MPEP § 2141.01)

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2'-(1H-tetrazol-5-yl)biphenyl-4-carbaldehyde is a well known intermediate and could be used for making a number of well known angiotensin II receptor antagonists, including the blockbuster drug valsartan. Valsartan is an angiotensin II receptor antagonist used to treat high blood pressure of congestive heart failure and post-myocardial infarction. It is currently marketed by Novartis under the trade name Diovan.

Daumas teaches the compound and process of making 2'-(1H-tetrazol-5-yl)biphenyl-4-carbaldehyde.

Ascertainment of the difference between the prior art and the claims (MPEP § 2141.02)

The difference between the prior art of Daumas and the instant claims is that the prior art is silent as to purity level.

Finding of prima facie obviousness – rationale and motivation (MPEP § 2142-2413)

However, in the absence of showing unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention when faced with Daumas that a pure compound can be made.

It is acknowledged that purer forms of a known product may be patentable, but the mere purity of a product, by itself, does not render the product unobvious. Ex parte Gray, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989). MPEP 2144.04. Factors to be considered in determining whether a purified form of an old product is obvious over the prior art include whether the claimed chemical compound or composition has the same utility as closely related materials in the prior art, and whether the prior art suggests the particular form or structure of the claimed material or suitable methods of obtaining that form or structure. In re Cofer, 354 F.2d 664, 148 USPQ 268 (CCPA 1966). (Claims to the free-flowing crystalline form of a compound were

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held unobvious over references disclosing the viscous liquid form of the same compound because the prior art of record did not suggest the claimed compound in crystalline form or how to obtain such crystals.).

Guided by the teachings of Daumas one of ordinary skill in the art would be able to make a purer compound of 2'-(1H-tetrazol-5-yl)biphenyl-4-carbaldehyde and its derivatives because the utility of the compounds is the same, i.e. that of an intermediate in making an angiotensin II antagonist, and Daumas teaches how to purify the product. One of ordinary skill would know that with routine experimentation a purer product can be obtained by recrystallizing the product several times to obtain a purer compound. It is routine experimentation that is predictable and easily recreated based on the teachings of Daumas.

The instant obviousness rejection is based on the close structural similarity of the instantly claimed compounds to the prior art compounds and the common utility shared among the compounds. There is an expectation among those of ordinary skill in the art that similar structural compounds will have similar properties and that modification of a known structure is mere experimentation within the means of a skilled artisan. See MPEP 2144.09(I). Therefore, the claims are rejected as obvious over the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being obvious over Daumas et al (US Patent No. 5,371,233 ('233 Pat) in view of Buhlmayer et al. (US Pat No. 5,399,578 ('578 Pat) or US Pat No. 5,965,592 ('592 Pat)).

Applicants claims relate to a process of making 2'-(1H-tetrazol-5-yl)biphenyl-4-carbaldehyde with a salt of an azide.

Determination of the scope and content of the prior art (MPEP § 2141.01)

Daumas teaches the compound 2'-(1H-tetrazol-5-yl)biphenyl-4-carbaldehyde and the process of making it using N-bromosuccinimide. (See columns 12-14, claims 11-14.)

Buhlmayer teaches a similar compound 2'-(1H-tetrazol-5-yl)biphenyl-4-ylmethyl)amide and the process of making using an azide. (See column 15, Process variant a, starting approximately line 31. Also see column 15, starting line 3, wherein it states that the salt forms of the starting materials may be used.)

Ascertainment of the difference between the prior art and the claims (MPEP § 2141.02)

The difference between the prior art and the instant claims is that the prior art of Daumas teaches the process for making the instantly claimed compound, while the prior art of Bulmayer teaches a similar intermediate (amide v. carbaldehyde) using the instantly claimed azide process.

Finding of prima facie obviousness – rationale and motivation (MPEP § 2142-2413)

However, in the absence of showing unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention when faced with the prior art to make the instantly claimed process. It is understood that the process of Buhlmayer is directed to an 2'-(1H-tetrazol-5-yl)biphenyl-4-ylmethyl)**amide** and its derivatives, while the instant claims are drawn to a 2'-(1H-tetrazol-5-yl)biphenyl-4-**carbaldehyde**. It is asserted that these two compounds are well known in the art as angiotensin II antagonists and one of ordinary skill in the art would be familiar with both of these intermediates and expect that they have the same properties, i.e. as angiotensin II antagonist intermediates. It would be considered experimentation on the part of a skilled artisan to use the process found in Buhlmayer for other well known intermediates that are similar in structure like the one instantly claimed. It is noted that the core compound of Buhlmayer, Daumas and the instant claims is the same, i.e. 1H-tetrazol-5-yl-biphenyl. Therefore, one of ordinary skill in the art would use the different processes taught to make the desired intermediate.

The selection of reaction conditions is more optimization by more modification of routine experimentation and within one skilled in the art. Changes in temperature, concentration, or both is not patentable modification in the absence of unexpected results which is different in kind and not degree. In re Aller, 105 USPQ 233. Discovery of an optimum value of a result effective variable is not patentable if such discovery is within one skilled in the art. A prima facie case of obviousness may be rebutted in optimizing a variable only when results are unexpectedly good. In re Boesch, 205 USPQ 215.

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Therefore, absent unexpected results, one of ordinary skill in the art would find the instant process mere experimentation when faced with Daumas in view of Buhlmayer.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Chung whose telephone number is (571) 272-6098.

The examiner can normally be reached on M-F, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Golam M. M. Shameem/
Primary Examiner, Art Unit 1626

Susannah Chung, 2/15/2009